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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,844	05/14/2001	Yi Hu	LEX-0176-USA	8344

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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/07/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/854,844	Applicant(s) HU ET AL.	
	Examiner Delia M. Ramirez	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-4 are pending.

Applicant's amendment of claims 1-3 in Paper No. 9, filed on 3/11/2002 and submission of a Declaration and Power of Attorney in Paper No. 10, filed on 3/11/2002 are acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 101

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

2. Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

3. Claims 1-4 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either an asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

4. This rejection has been discussed in previous Office Action Paper No. 7, mailed on 12/3/2001.

5. It is noted that due to a typographical error, claim 4 was not included in the group of claims rejected under 35 U.S.C. 101 in previous Office Action Paper No. 7, mailed on 12/3/2001.

6. Applicants have extensively argued that the polynucleotides of the instant invention have substantial, credible, specific and well-established utility. Applicants argue that a claim does not need to describe the invention, such description being the role of the disclosure, and that there is no statutory requirement for the disclosure of a specific example. Applicants also argue that the closest homologs used by the Examiner for sequence comparison and function determination (Yamada et al., SPTREMBL accesion number Q9PVX7, May 1, 2000 ; GenEMBL accesion number AB018694, October 5, 1999) are not the proper homologs to compare the polypeptide and polynucleotide of the instant application with, and that GENBANK's entry XM_093852, which Applicants assert is a serine protease, presents a 99% sequence homology to the polypeptide of the instant application. Therefore, Applicants assert, one of skill in the art would believe that the polypeptide encoded by the polynucleotide of the instant application is a serine protease. Further, Applicants assert that the instant polynucleotide have a number of substantial and credible utilities such as being used in DNA chips as specific markers of the human genome and expanding the utility of data coming from the human genome project as it relates to the discovery of drugs and human therapeutics.

7. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the utility rejection. The utility rejection was not applied due to the lack of a specific example or because the claims do not describe the invention. As Applicants have indicated, a claim does not need to describe the invention and that there is no statutory requirement for the

disclosure of specific examples. The statements made in the previous Office Action (Paper No. 7) in regard to these issues were intended to clarify what was disclosed and what was not disclosed in the instant application.

8. In regard to the arguments presented by Applicants as they relate to the function of the polypeptide encoded by the polynucleotide of the instant invention, it is noted that the Examiner has not found the GENBANK entry provided by Applicants and no alignment of the polypeptide of SEQ ID NO: 2 (instant application) with that GENBANK entry has been provided by Applicants either. The homologs presented by the Examiner in the previous Office Action (Yamada et al., SPTREMBL accesion number Q9PVX7, May 1, 2000 ; GenEMBL accesion number AB018694, October 5, 1999) were the closest homologs found. Applicants are invited to provide alignments as evidence to support Applicant's assertion of serine protease function.

9. In regard to the additional utilities that Applicants have asserted as substantial, credible, and well-established, it is noted that those utilities would be applicable if one of skill in the art know which is the substrate and specificity of the alleged serine protease. Neither the specification nor the current state of the art discloses the substrate and specificity of the polypeptide (SEQ ID NO: 2) encoded by the polynucleotide (SEQ ID NO: 1) of the instant application. Serine proteases belong to a very diverse family with different substrates and specificities. Therefore, it is not clear how one can use the polynucleotide of the instant application in the search for human therapeutics with the information provided. Applicant's asserted utility for the polypeptide (serine protease) encoded by the polynucleotide of the instant application, particularly in view of a lack of information in regard to substrate and specificity, constitutes a utility that requires further research to identify or reasonably confirm a "real world"

context of use. See e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). This type of utility is not considered a "substantial utility". An assay that detects the presence of an agent that has a stated correlation to a predisposition to the onset of a specific disease condition would be considered a "substantial utility" in the context of identifying potential candidates for preventive measures. Here, the polypeptide and the corresponding polynucleotide disclosed are suitable only for additional research. Thus, applicants have not disclosed a specific and substantial utility for the claimed polynucleotide.

10. **In case Applicant overcomes this utility rejection by providing convincing evidence in response to this Office Action, the following rejections will apply:**

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claim 2 is indefinite in the recitation of "an isolated nucleic acid molecule comprising a nucleotide sequence that: (a)....; and (b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof." for the following reasons. First, it is not clear how a sequence can hybridize to another sequence since hybridization, as known in the art, occurs between nucleic acid molecules. Second, the term "complement"

renders the claim indefinite because it is unclear which "complements" are encompassed by the claims. Fragments of any size which are complementary to the polynucleotides claimed can be considered as "complements". Applicants have not define the term "complement", as it relates to size, in the specification either. If applicants wish to claim the entire complementary sequence, it is suggested that the term "complement" be replaced with "complete complement".

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

14. This rejection has been discussed in previous Office Action Paper No. 7, mailed on 12/3/2001.

15. Applicants extensively argue that adequate description of the claimed genus has been provided in the specification. Specifically, Applicants argue that the nucleic acid sequences provided is sufficient to allow one of skill in the art to distinguish the genus from other materials, and that, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.*, the nucleic acid sequences of the present invention are not distinguished by function but by

structural elements, i.e. the sequence itself. Therefore, polynucleotides comprising at least 24 contiguous bases from SEQ ID NO: 1 are within the described genus and polynucleotides which lack this structural feature lie outside the genus.

16. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. While it is acknowledged that the current claims differ from those held by the court to lack sufficient written description in that the instant claims recite the genus of polynucleotides claimed in structural terms and not in functional terms, as discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. The claim, as written, encompasses a genus of polynucleotides comprising at least 24 nucleotides of SEQ ID NO: 1 wherein said polynucleotides encode polypeptides of <u>any function</u>. The specification discloses the structure (sequence) of the polynucleotide of SEQ ID NO: 1 and <u>one function</u> for the corresponding polypeptide (SEQ ID NO: 2). As indicated

previously, many functionally unrelated polypeptides are encompassed by the claim. In the instant case, the specification only discloses a single species of the claimed genus, therefore one cannot reasonably conclude that Applicants had possession of the claimed invention at the time the instant application was filed.

17. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

Claim 1 is so broad as to encompass any polynucleotide encoding a polypeptide of any function wherein the polynucleotide comprises a fragment of at least 24 nucleotides of SEQ ID NO: 1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides encoding polypeptides of unknown function broadly encompassed by the claim. While the specification discloses the sequence and function of the polypeptide of SEQ ID NO: 2 and the corresponding polynucleotide (SEQ ID NO: 1), no disclosure of the function or structure of polypeptides encoded by polynucleotides comprising at least 24 contiguous nucleotides of SEQ ID NO: 1 has

been provided. The specification does not disclose any information about the critical structural elements within the nucleotide sequence of SEQ ID NO: 1 that are required to maintain the desired function such as the catalytic domain, the binding domain, and the like. No examples of other polynucleotides comprising at least 24 contiguous bases of the sequence set forth in SEQ ID NO: 1 encoding polypeptides with the desired function are provided either.

The current state of the art indicates that small amino acid changes can drastically change the function of a polypeptide and that annotation of function based on sequence identity may lead to inaccurate predictions. Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995; cited in previous Office Action) teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* where found to be hydroxylases once tested for activity. As taught by Broun et al. (Science 282:1315-1317, 1998; cited in previous Office Action), as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase into a desaturase. The amino acid sequence of the polypeptide determines its structural and functional properties, therefore, one of skill in the art would require some knowledge and guidance as to how structure is related to function in order to determine if a polypeptide encoded by a polynucleotide comprising at least 24 nucleotides of SEQ ID NO: 1 has the desired activity. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to maintain the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate those molecules, as encompassed by the claim, with the desired activity. Thus, Applicant has not provided sufficient

guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Conclusion

18. No claim is in condition for allowance.

19. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

20. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of

a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
May 3, 2002

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